UPDATE HEPATITIS B IMMUNIZATION

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Discolosures

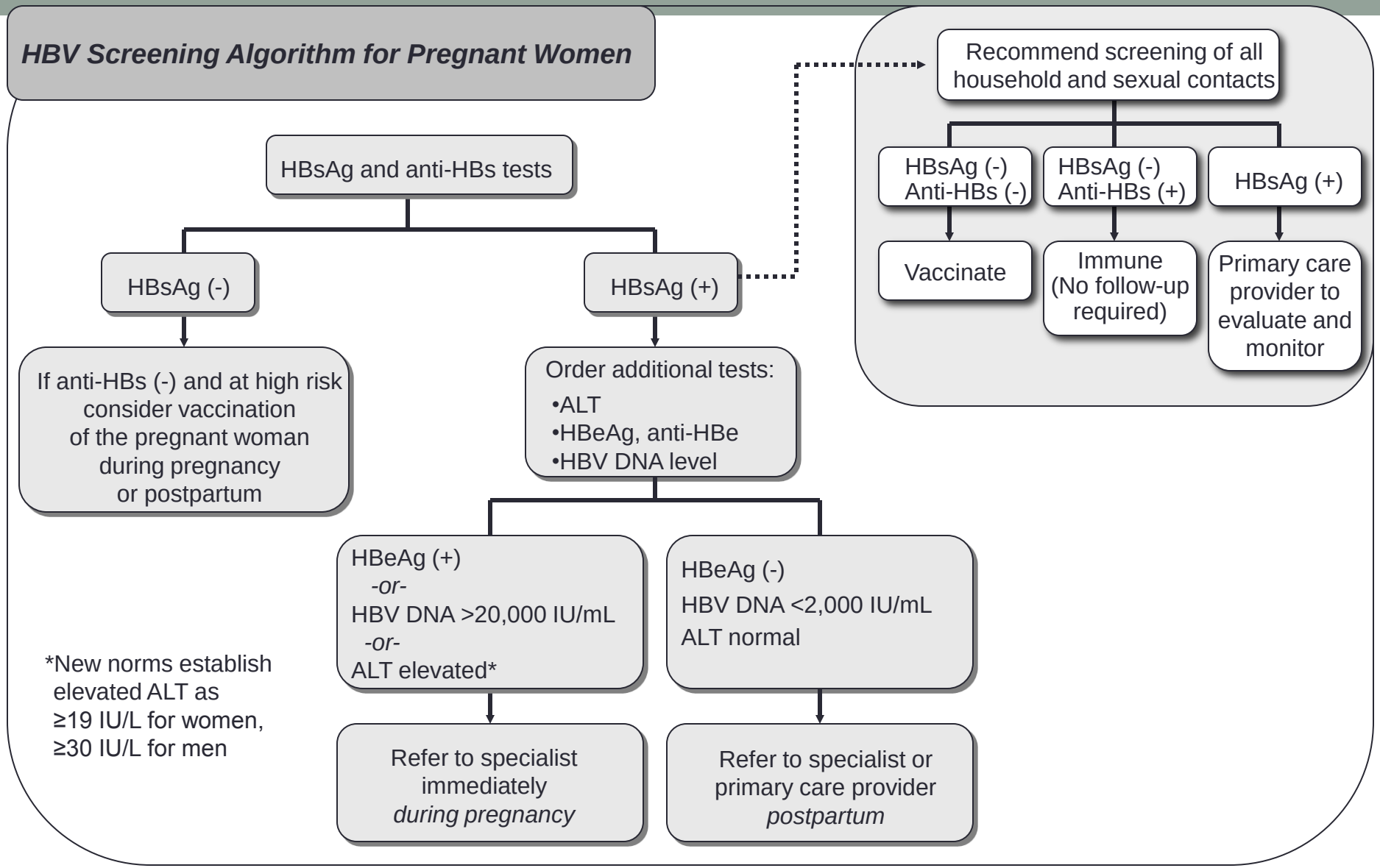
- No disclosures
- I will mention non licensed hepatitis B vaccine

Goals of Presentation

- Understand the epidemiology of hepatitis B virus (HBV) infection in the US
- To review screening recommendations for pregnant women for HBV infection
- To discuss the importance of the birth dose
- To understand the impact of infant and childhood hepatitis B vaccination programs in Alaska and the USA
- To discuss new recommendations for the administration of hepatitis B vaccine in adults
- To review data from Alaska Study on how long protection from hepatitis B vaccine lasts in adults and children

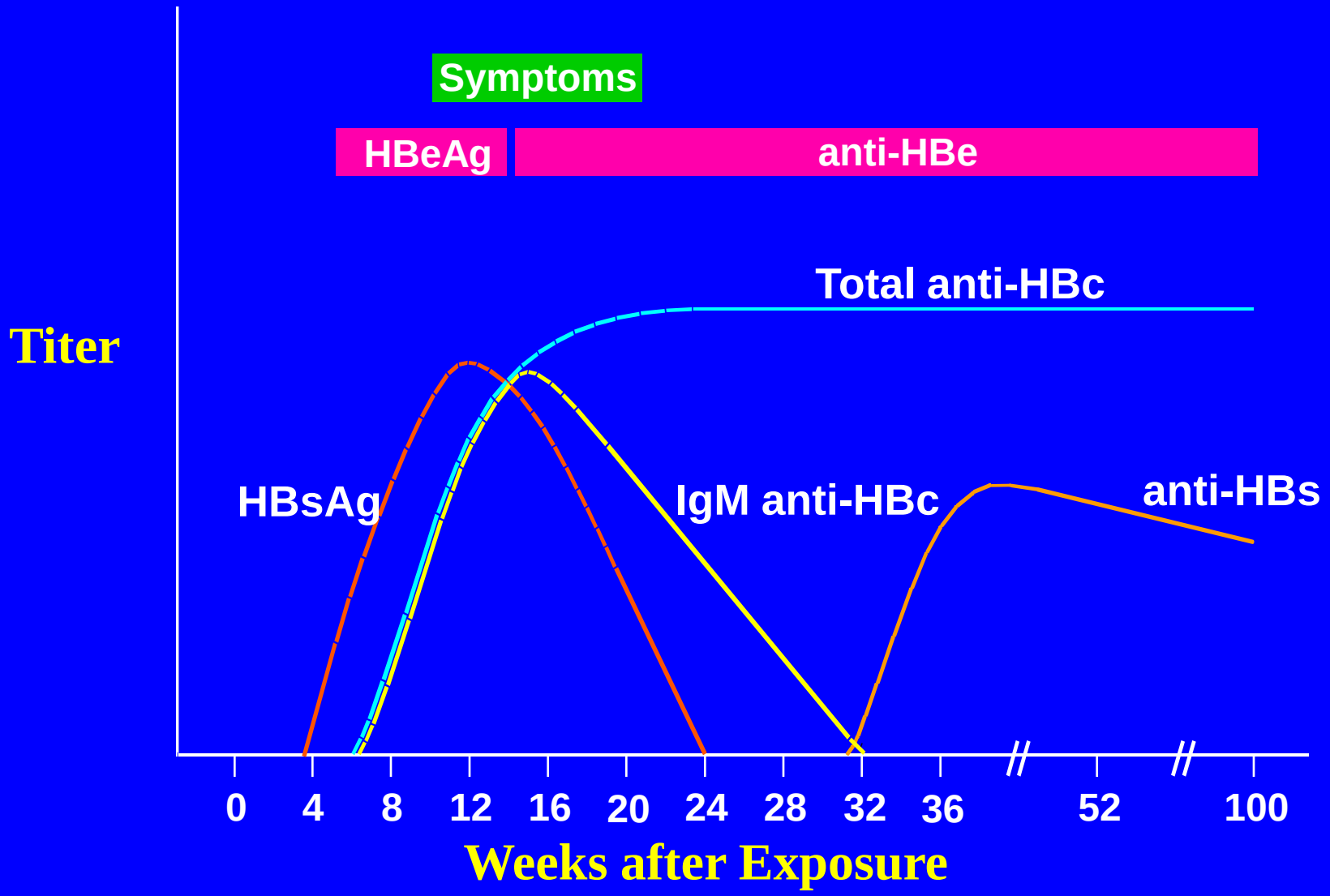
Pop Quiz

- 35 y.o. Mother who was born in the Philippians and come to US at age 5 who is negative for HBsAg. She is married to a US born Caucasian male. All of her children have been vaccinated against HBV. Her provider tells her that since she is HBsAg-negative she would suggest waiting until the baby is 2 months old to start hepatitis B vaccine. The mother is a stay at home mom.
  a) The child is at not risk of HBV infection in the 1st 2 months of life and this is perfectly acceptable option
  b) The child is at a remote risk of HBV infection but the risk benefit ratio of vaccination allows the option to delay vaccine
  c) This child could conceivable be at risk for HBV infection
  d) A very low risk of autism makes it a smart decision to refer vaccination

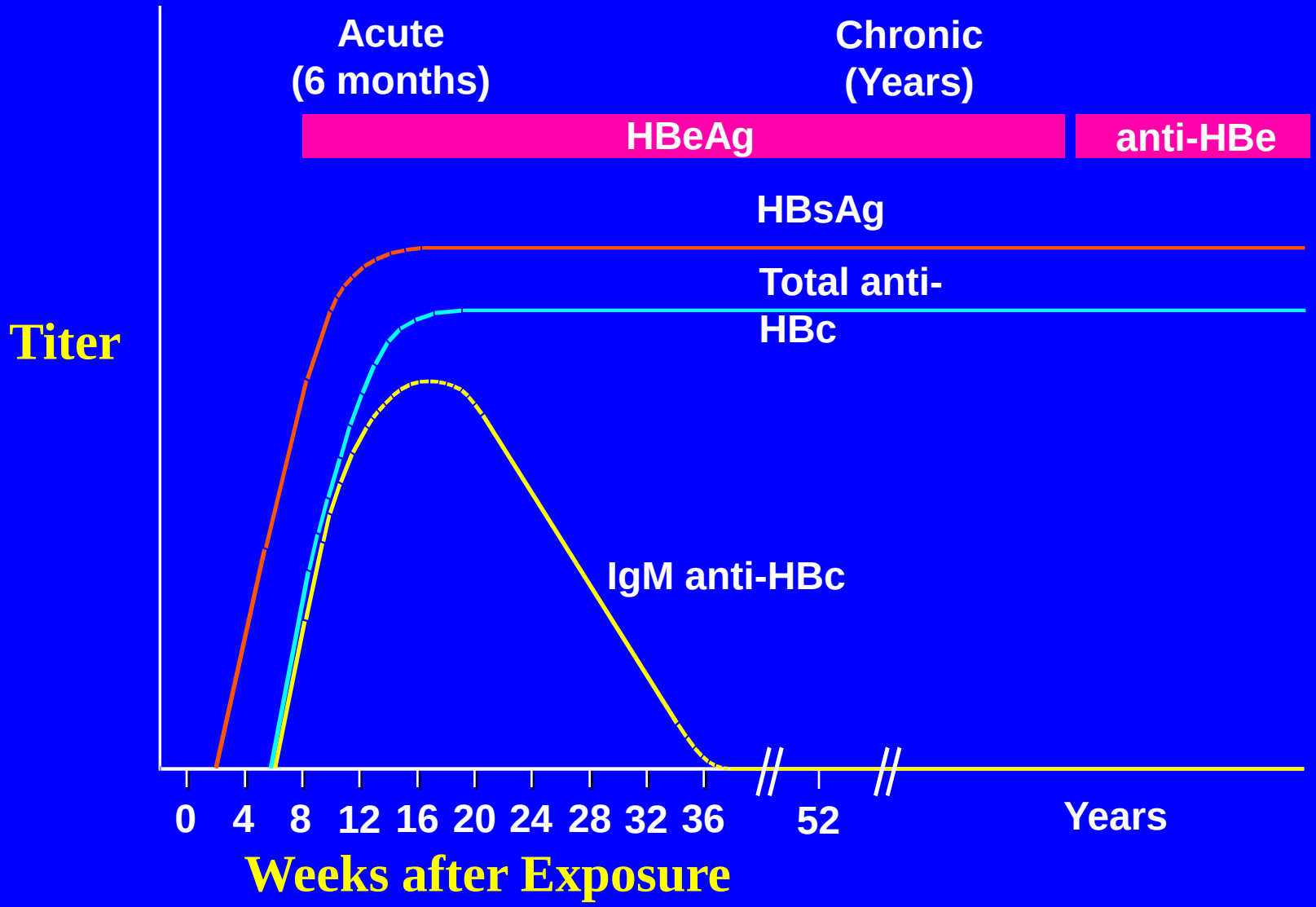


Apuzzio J, et al. The Female Patient 2012;37(5):30-4

Acute Hepatitis B Virus Infection with Recovery



Acute Hepatitis B Virus Infection with Progression to Chronic Infection



Primary Modes of HBV Transmission by Age Group

Age Group	Primary Mode of Transmission
Birth	• Perinatal
Early childhood	• Unsafe injections • Inapparent parenteral*
Late childhood, adolescence, adulthood	• Unsafe injections • Sexual • Injection drug use

* From family member to child or child to child, through inapparent exposure to HBV infected blood from open cuts

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Rates of Symptomatic and Chronic HBV by Age at Infection

Age at infection	Symptomatic HBV Infection	Chronic HBV
< 1 year	< 1 %	90%
1 – 5 years	5 – 15%	25 - 50%
>5 years	20 – 50%	6 – 10%

McMahon BJ, J Infect Dis 1985;151:599
Edmonds WJ Proc R Soc Lond B Biol Sc 1993; 253:197
Hyams KC. Clin Infect Dis 1995;20:992

2 Modes of HBV Transmission in Infancy and Early Childhood

- "Vertical" …. from infected mother during pregnancy or delivery (perinatal infections)
- "Horizontal"…. from infected household member or close contact

Perinatal Transmission

- Transmission from infected mother to infant
  - Predominantly occurs in HBV genotype C
- Occurs through percutaneous and permucosal exposure to mother's blood
- Usually occurs during birth
- *In utero* transmission rare: accounts for ~5% of perinatal infections
- HBV **not** transmitted by breastfeeding

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Risk of Perinatal HBV Transmission by HBeAg Serostatus of Mother

Serostatus of Mother		% Infants Infected
HBsAg	***HBeAg***	
Positive	Positive	85% -100%
Positive	Negative	5% - 30%*

Depends on level of HBV DNA

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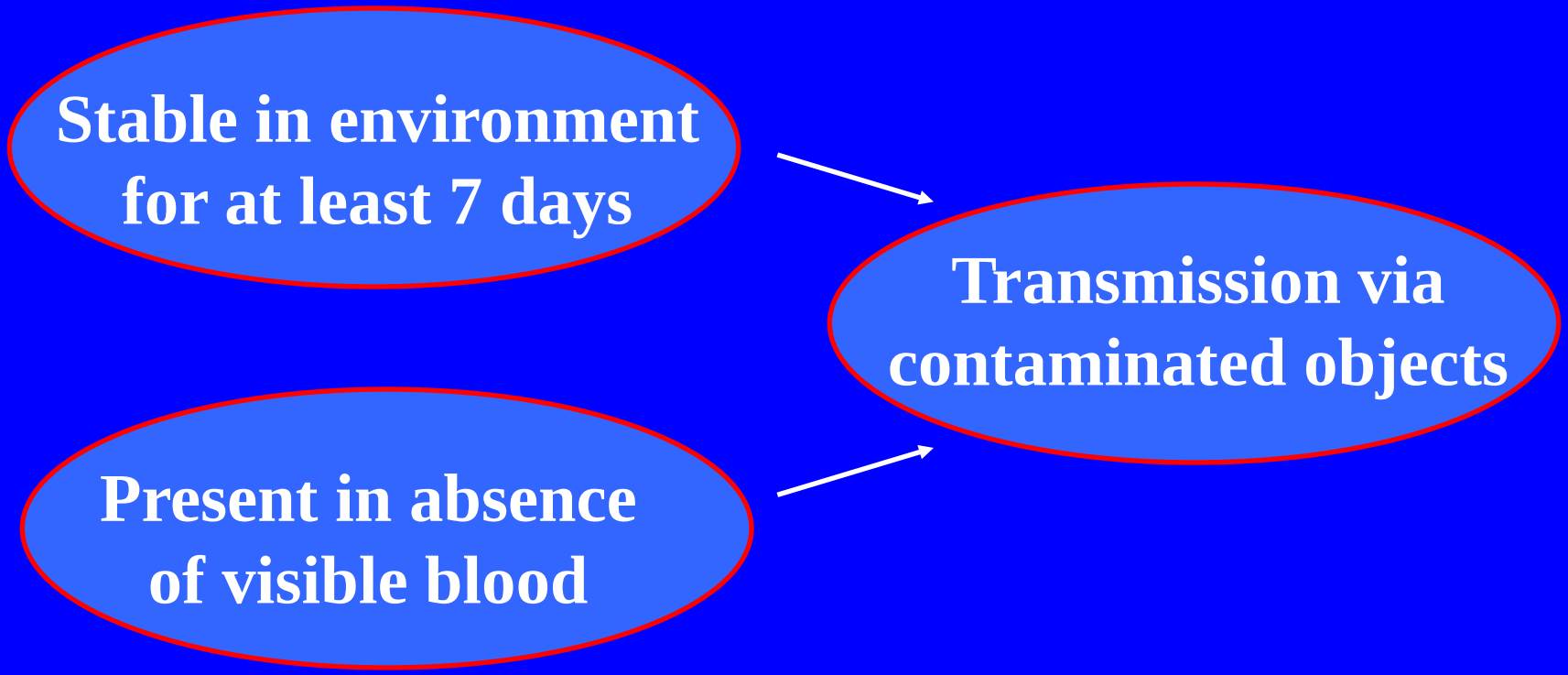
Perinatal HBV Infection in the USA

- According to a report in 2010 by the Institute of Medicine, an estimated 1,000 infants in the US per year develop chronic hepatitis B infection:
  - 2 primary reasons are:
    - Lack of screening of mother for HBsAg
    - Failure to give birth dose, especially when mother has not been previously screened. >90% of HBV transmission can be prevented by giving the birth dose followed by completing immunization schedule
  - Other reasons included:
    - Very high HBV DNA viral load in mother (> 10 log copies/ml)
      - Antiviral prophylaxis of mother may prevent this from occuring
    - Failure to give HBIG post delivery

HBV in the Environment

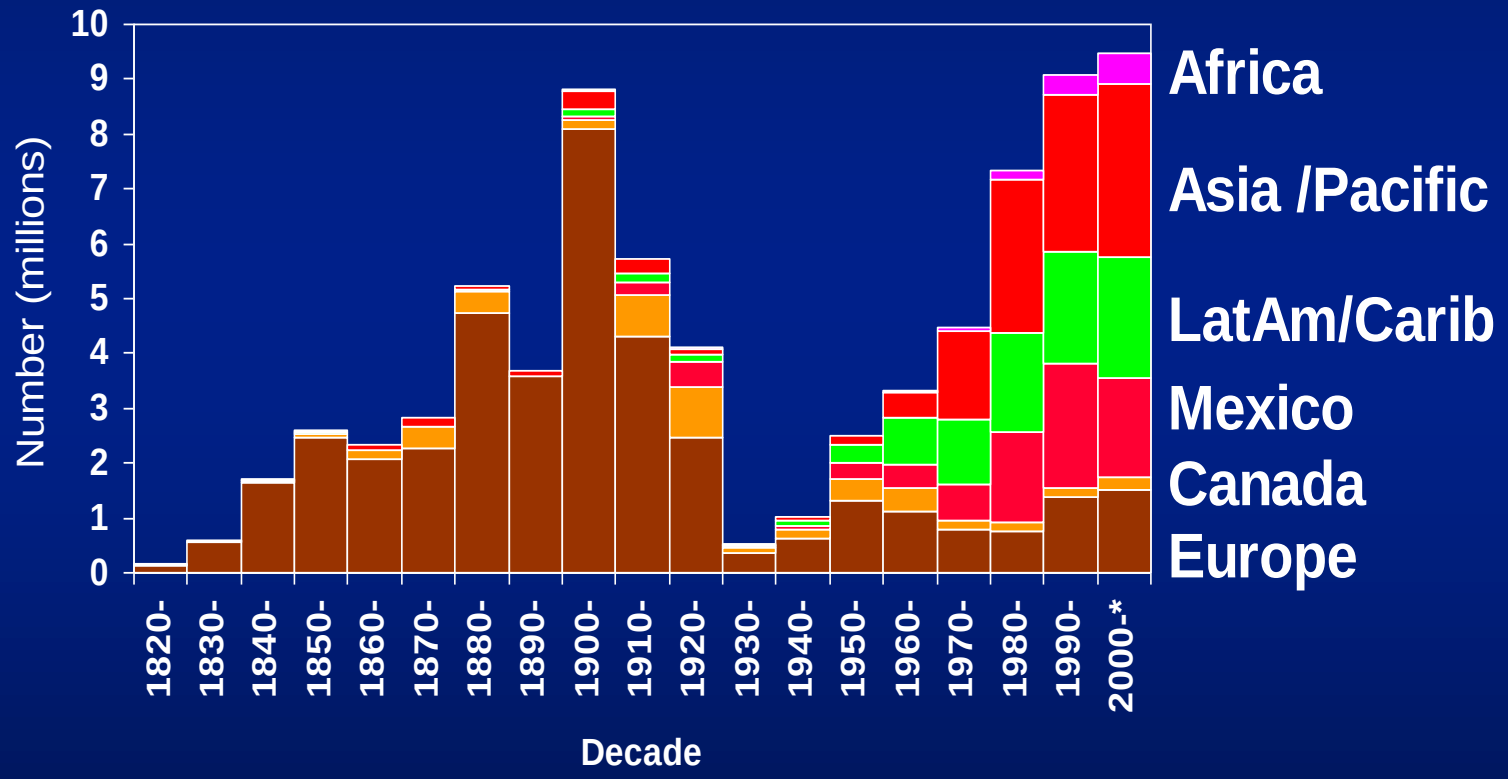


Horizontal HBV Transmission during Early Childhood (0 – 5 Years)

- Contact with HBV in body fluids (blood, serum, saliva) from infected household members (including mother) or contact with contaminated surfaces
- Transmission via breaks in skin, e.g., injuries or dermatitis, or via mucosal exposures, e.g., sharing tooth brushes
- HBV resistant to drying, alcohol; remains stable on environmental surfaces for ~ 7 days
- Pre-exposure vaccination starting at birth is best prevention of horizontal HBV transmission

Bond WW Lancet 1981;1(8219):550
Bancroft WH J Infect Dis 1977;135:79
Beasley RP J Infect Dis 1983;147:85

Changing Patterns of U.S. Immigration 1820-2004



*Projected based on 2001-2004 data

Source: Yearbook of Immigration Statistics, 2004

Recombinant Hepatitis B Vaccine Efficacy (VE) among Infants Born to HBsAg, HBeAg-Positive Women by Vaccine Type and Dosage

Country	HBIG	Hepatitis B Vaccine Efficacy Without and With HBIG Ages 0, 1, 6 months		Other Dosages & Schedules
Burma Thailand	No	MSD 5 ug	93% 86%-89%	59%-79%
Thailand		GSK 10 ug	92%	95%
Thailand USA	Yes	MSD 5 ug	89% 92%	88%-97%
Thailand Taiwan		GSK 10 ug	100% 90%	89%-98%

Pongpipat D. 1989; Stevens CE. 1975, 1979;1985,1992. Lee C-Y. 1991, 997; Poovorawan Y. 1989; 997; 2009; Lolekha S. 2002; Mast E. *Vaccine, Eds.* Orenstein W, Plotkin S, 2004.

Hepatitis B Vaccines

- Available since 1981
- Composed of HBsAg adsorbed to aluminum hydroxide
- Elicits development of neutralizing antibodies to HBsAg (anti-HBs) which confer protection from infection
- Plasma-derived and recombinant formulations

Administration of Hepatitis B Vaccine

- Typically given as a three dose series
  - Four dose series used routinely in Alaska because of combination DTaP-HepB-IPV (Pediarix)
  - Schedule flexible
  - 0,1-2,6 month schedule most commonly used
- Microgram dose varies by manufacturer and age of recipient
- Vaccines can be used interchangeably if given at dose recommended by manufacturer

Four Doses of Hepatitis B Vaccine vs. Three Doses

- Excellent protection (>95%) is provided with 4 doses of hepatitis B vaccine
- A fourth dose does not improve seroconversion rate but would provide higher level of anti-HBs post vaccination series
- Unfortunately, well conducted randomized controlled studies comparing 3 to 4 doses of vaccine are not available
- There is absolutely no harm to getting a fourth dose of hepatitis B vaccine for either an infant or an adult
  - However, extra doses for adults are not needed; documentation of receiving 3 doses of vaccine at any time is sufficient

Hepatitis B Vaccine Safety

- Hepatitis B vaccine administered to millions of infants, children and adults worldwide
- Side effects rare
- Anaphylaxis estimated to occur in 1 per 600,000 doses administered
- No scientific data linking hepatitis B vaccine and
  - multiple sclerosis
  - other autoimmune diseases
  - Autism

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Summary of Rationale for Universal Birth Dose of Hepatitis B Vaccine

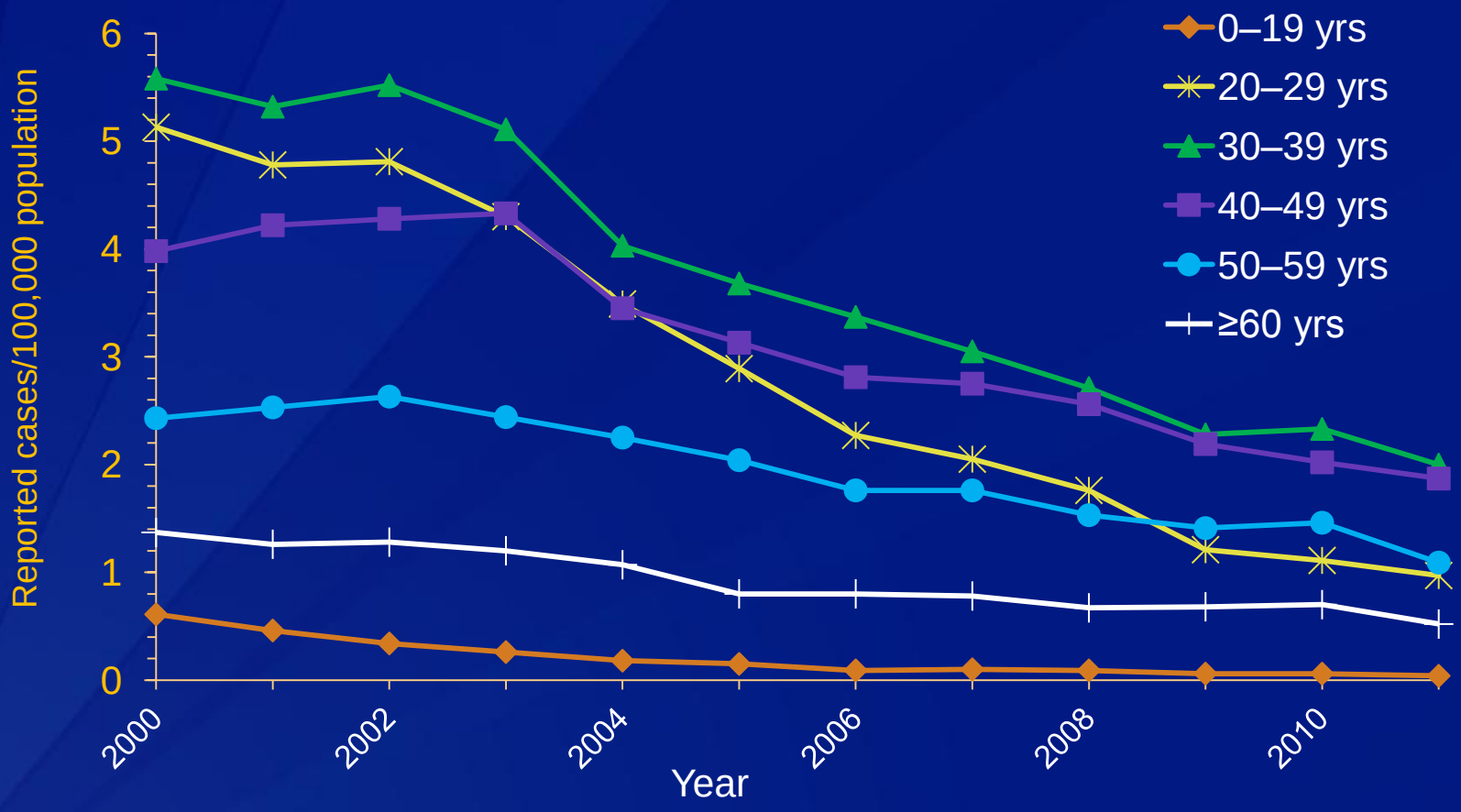
- Prevents most vertical HBV transmission to infants born to HBsAg-positive women, and
- Provides "safety net" for infants whose mother's status unknown or uncertain at delivery
- Prevents horizontal HBV infection during childhood regardless of HBsAg-status of mother & contacts
- First dose at birth results in higher rates of on-time completion of hepatitis B series, other vaccines*

***Jacques-Carroll L et al. Arch Pediatr Adolesc Med 2009;163: 489**

Figure 3.1. Reported number of acute hepatitis B cases — United States, 2000–2011

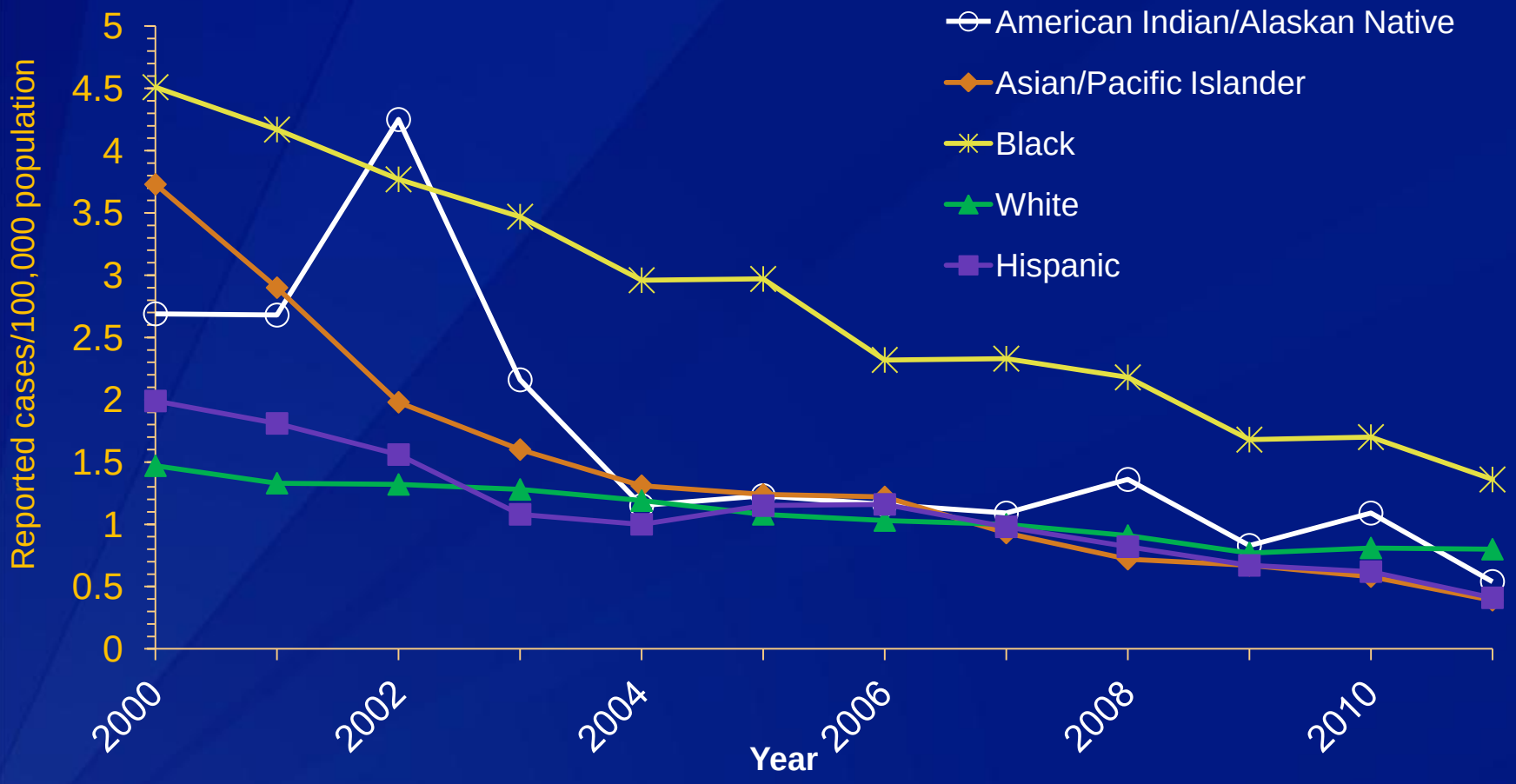
Source: National Notifiable Diseases Surveillance System (NNDSS)

Figure 3.2. Incidence of acute hepatitis B, by age group — United States, 2000–2011



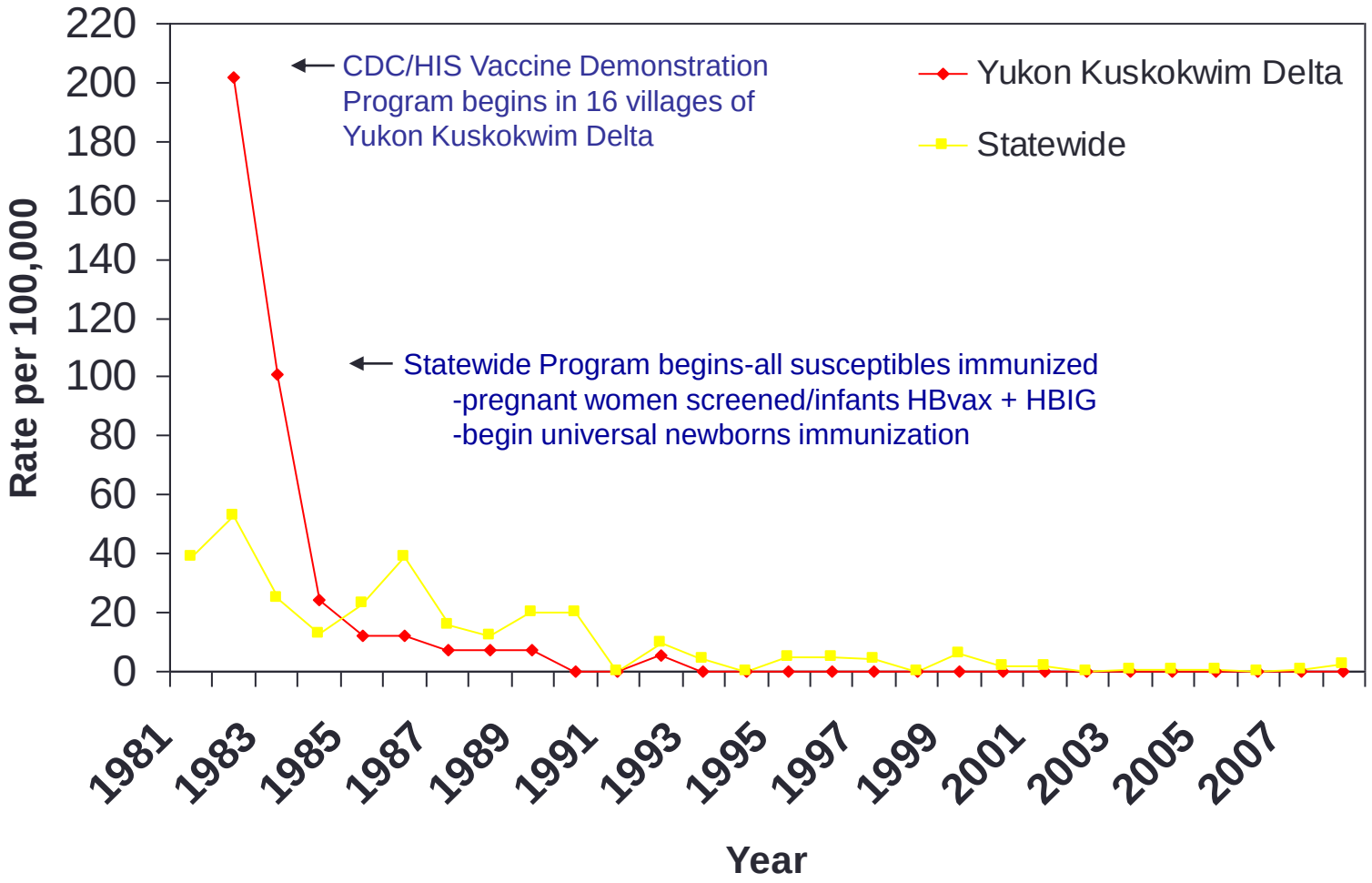
Source: National Notifiable Diseases Surveillance System (NNDSS)

Figure 3.4. Incidence of acute hepatitis B, by race/ethnicity — United States, 2000–2011



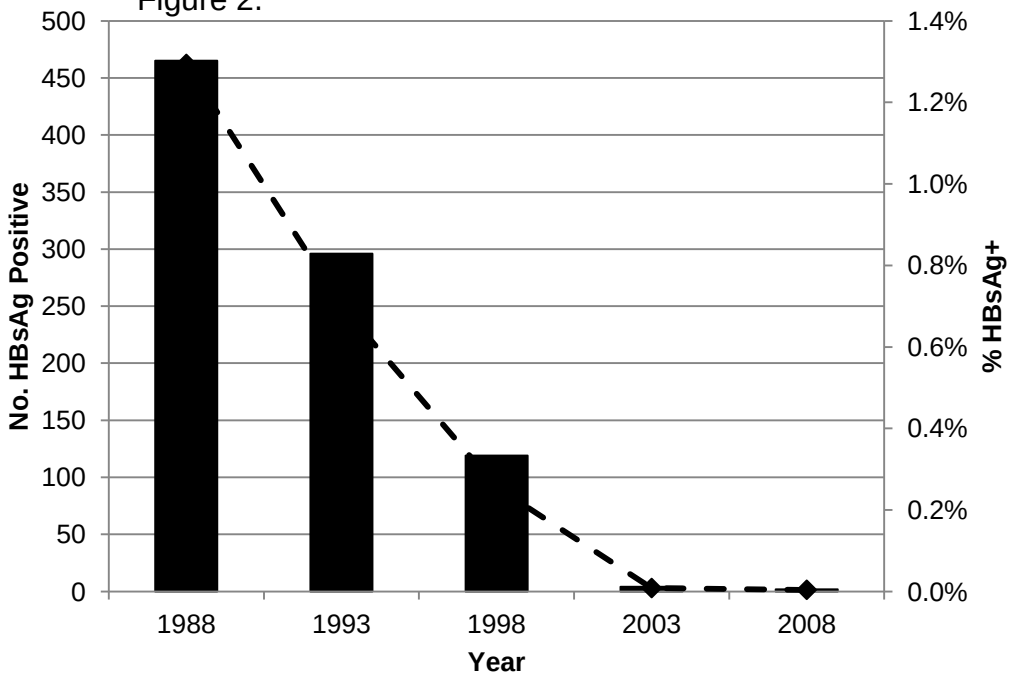
Source: National Notifiable Diseases Surveillance System (NNDSS)

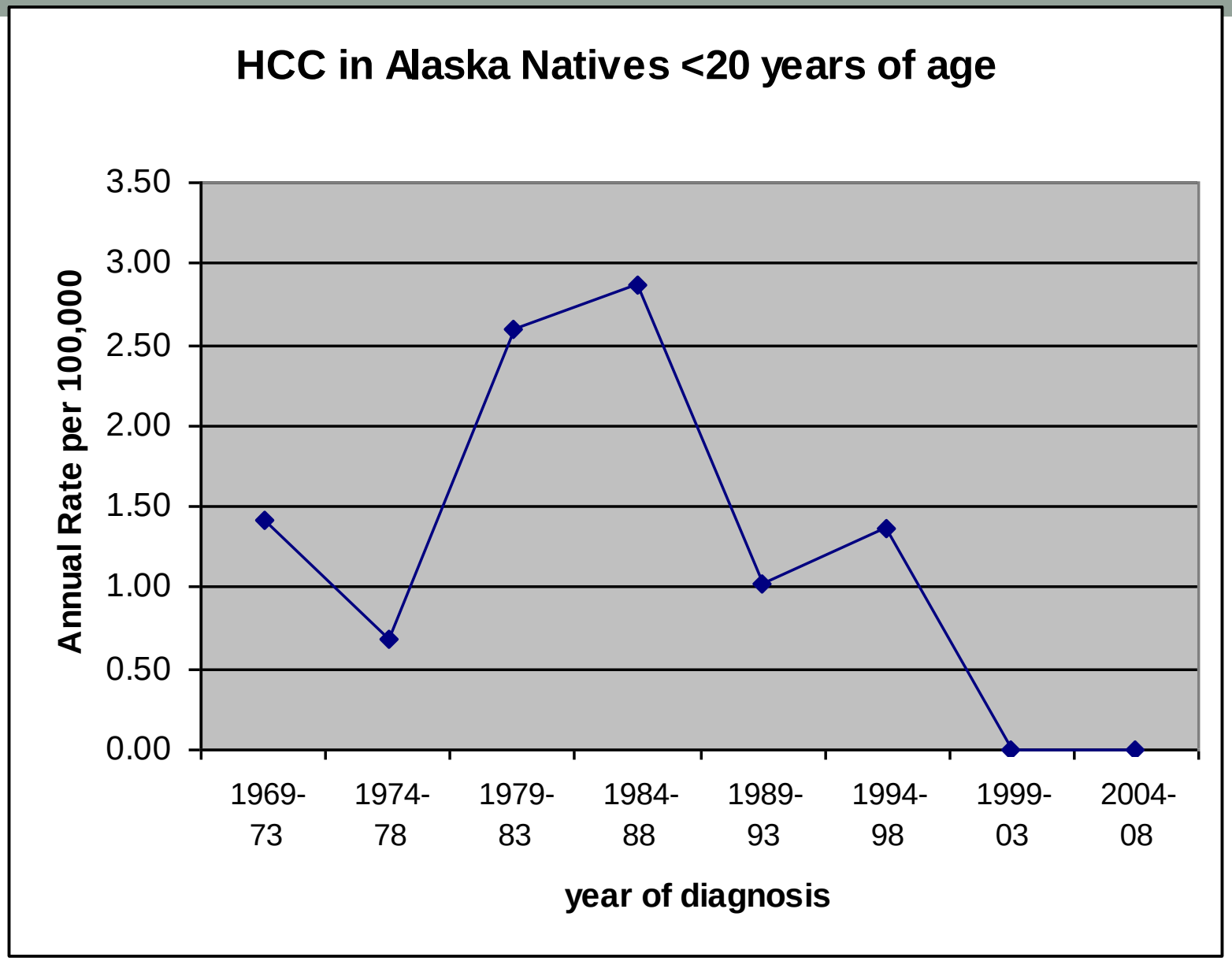
Incidence Symptomatic Hepatitis B in Alaska Native Peoples 1981- 2008



Number of HBsAg-positive Alaska Native Children Under 20 Years of Age: 1988-2008

Figure 2.





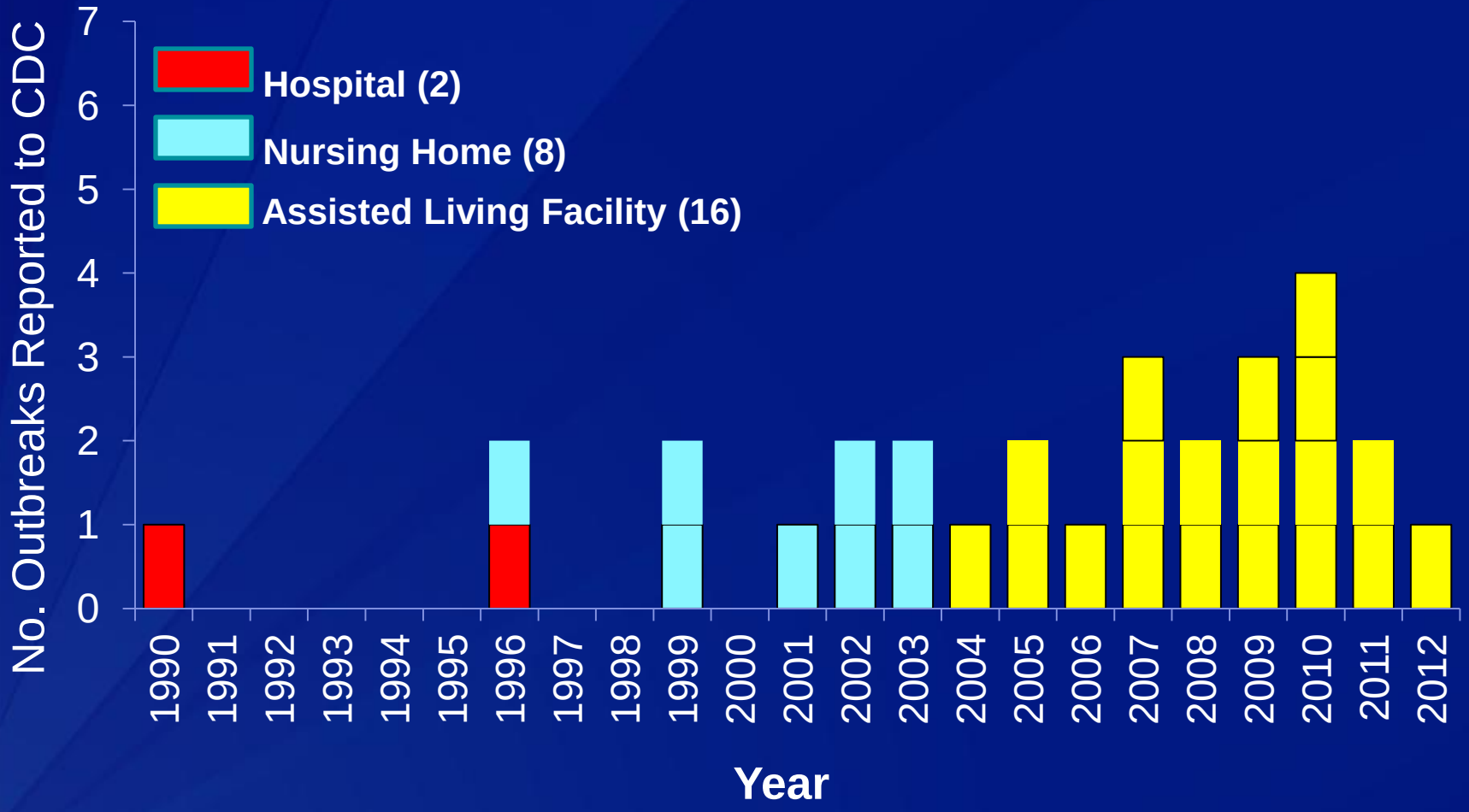
P value for trend = 0.002

Hepatology 2011;54:801-7

Does Hepatitis B Vaccine Provide Long-term Protection from HBV Infection?

- Persons fully vaccinated in child or adulthood who responds is protected form subsequently acquiring acute symptomatic hepatitis B and developing the chronic carrier state for at least 30 years after vaccination
- Infants who respond to hepatitis B vaccine are also protected for up to 20 years, though anti-HBs is likely to have disappeared and they may not respond to a booster dose
  - Cellular immunity likely provides long-term protection
    - Breakthrough infections are reported to not result in symptomatic infection or lead to chronic carrier stage
    - Recent study shows persons exposed after blood transfusion to HBV who were vaccinated had rapid development of innate immunity
    - Infants in Taiwan who received an incomplete vaccination series starting at birth had decrease risk of subsequent acute hepatitis and HCC compared to unvaccinated infants

Outbreaks of Hepatitis B Virus Infection among Persons with Diabetes with Blood Glucose Monitoring, 1990-2012



Transmission of Hepatitis B Virus (HBV) during Blood Glucose Monitoring

Infected with HBV

Indirect person to person contact transmission

Infected with HBV

Blood contaminated equipment/supplies (includes no visible blood); HBV infectious for >7 days

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Pop Quiz

- Correct Answer:
  - c) This child could conceivable be at risk for HBV infection
  - WHY?
    - There is a large extended family most of whom were born in the Philippine Islands
    - Mom is getting pressure to bring baby over to see relatives in the Philippine Islands when the baby is 4-6 weeks old
  - What could the provider do if she does not want to give the birth dose?
    - Investigate all family members and friends from mom's family to make sure they were screened and vaccinated and urge no contact with any members found to be HBsAg+
    - Tell her she absolutely cannot go the Philippine Islands now.
    - Strict isolation for mother and child till child is 8 weeks old and gets 1st dose of vaccine.

Hepatitis B: What Hospitals Need to Do to Protect Newborns

http://www.immunize.org/protect-newborns/guide/birth-dose.pdf